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March 1, 2004

Commissioner for Patents
P.O. Box 1450
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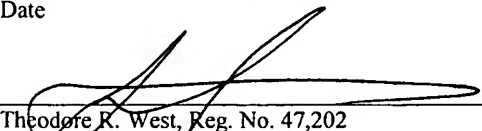
Re: U.S. Patent Application No.: 10/731,463
For: *Amidine Derivatives for Treating Amyloidosis*
Inventors: Chalifour, Robert J. *et al.*
Filed: December 5, 2003
Our Ref. No.: NBI-105CN

Dear Sir:

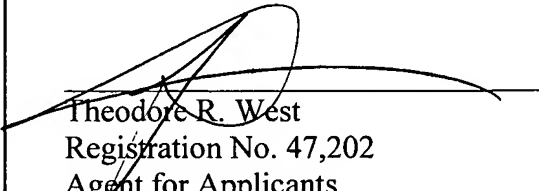
I enclose herewith for filing in the above-identified application the following:

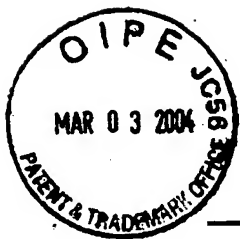
1. Information Disclosure Statement (2 pages, in duplicate);
2. PTO Form 1449 (6 pages);
3. Copies of references cited in said PTO Form 1449 (180 references);
4. A copy of the International Preliminary Examination Report from PCT/CA02/01353 (9 pages); and
5. A Return Postcard.

No additional costs are believed to be due in connection with the filing of this Information Disclosure Statement. However, please charge any necessary fees in connection with the enclosed statement to our Deposit Order Account No. 12-0080. For this purpose, a duplicate of this sheet is attached.

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Date	March 1, 2004
	
Theodore R. West, Reg. No. 47,202	

Respectfully submitted,
LAHIVE & COCKFIELD, LLP


Theodore R. West
Registration No. 47,202
Agent for Applicants



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the application of: Chalifour, Robert J. *et al.*

Serial No.: 10/731,463

Filed: December 5, 2003

For: *AMIDINE DERIVATIVES FOR TREATING
AMYLOIDOSIS*

Attorney Docket No.: NBI-105CN

Group Art Unit: 1621

Examiner: Not Yet Assigned

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Certificate of First Class Mailing (37 CFR §1.8(a))

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Date of Signature and of Mail Deposit

By: 

Theodore R. West
Registration No. 47,202
Agent for Applicants

INFORMATION DISCLOSURE STATEMENT

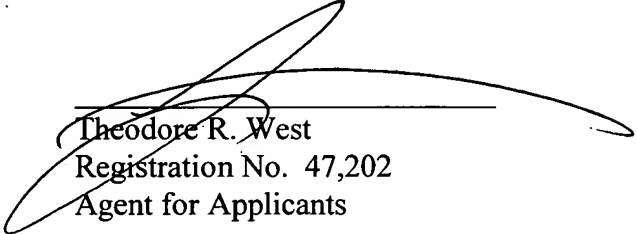
Dear Sir:

Applicants and their representatives are aware of the following publications and information, listed on the attached PTO Form 1449, and in accordance with 37 CFR §1.97 hereby submit these publications for the Examiner's consideration. Reference ID Nos. A28, C14, C17, D9, D21, E13, E14, E1, E20, F4, F7, F17, and F18 were cited in an International Preliminary Examination Report during the prosecution of PCT/CA02/01353 dated September 12, 2003, which relates to the above-referenced application. A copy of the report and each cited publication is enclosed.

This statement is not to be interpreted as a representation that the cited publications are material, that an exhaustive search has been conducted, or that no other relevant information exists. Nor shall the citation of any publication herein be construed *per se* as a representation that such publication is prior art. Moreover, Applicants understand that the Examiner will make an independent evaluation of the cited publications.

No additional costs are believed to be due in connection with the filing of this Information Disclosure Statement. However, please charge any necessary fees in connection with the enclosed statement to our Deposit Order Account No. 12-0080..

Respectfully submitted,
LAHIVE & COCKFIELD, LLP



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Date: March 01, 2001

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APPLICANT FACSIMILE OF FORM PTO-1449

U.S. DEPARTMENT OF
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PATENT AND TRADEMARK
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ATTY DOCKET NO

SERIAL NO.

NBI-105CN

10/731,463

LIST OF PUBLICATIONS CITED BY APPLICANT
(Use several sheets if necessary)

APPLICANT

Chalifour, et al.

FILING DATE

GROUP

December 5, 2003

1621

U.S. PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE
	A1	4,324,794	Apr-82	Tidwell <i>et al.</i>	514	387	
	A2	4,397,863	Aug-83	Tidwell <i>et al.</i>	514	415	
	A3	4,515,625	May-85	Burow, Jr.	71	92	
	A4	4,522,811	Jun-85	Eppstein, <i>et al.</i>	514	2	
	A5	4,619,942	Oct-86	Tidwell, <i>et al.</i>	514	415	
	A6	4,933,347	Jun-90	Tidwell, <i>et al.</i>	514	256	
	A7	4,940,723	Jul-90	Tidwell, <i>et al.</i>	514	396	
	A8	4,963,589	Oct-90	Tidwell, <i>et al.</i>	514	636	
	A9	5,202,320	Apr-93	Tidwell, <i>et al.</i>	514	218	
	A10	5,206,236	Apr-93	Tidwell, <i>et al.</i>	514	218	
	A11	5,246,965	Sep-93	Main	514	532	
	A12	5,374,548	Dec-94	Caras	424	450	
	A13	5,387,742	Feb-95	Cordell	800	12	
	A14	5,399,311	Mar-95	Kasai, <i>et al.</i>	419	28	
	A15	5,428,051	Jun-95	Tidwell, <i>et al.</i>	514	394	
	A16	5,441,870	Aug-95	Seubert, <i>et al.</i>	435	7.1	
	A17	5,451,700	Sep-95	Morrissey <i>et al.</i>	564	165	
	A18	5,521,189	May-96	Boykin <i>et al.</i>	514	256	
	A19	5,538,845	Jul-96	Knops, <i>et al.</i>	435	6	
	A20	5,547,841	Aug-96	Marotta, <i>et al.</i>	435	6	
	A21	5,552,426	Sep-96	Lunn, <i>et al.</i>	514	394	
	A22	5,574,059	Nov-96	Regunathan <i>et al.</i>	514	397	
	A23	5,578,631	Nov-96	Tidwell, <i>et al.</i>	514	394	
	A24	5,594,138	Jan-97	Dykstra, <i>et al.</i>	540	596	
	A25	5,602,172	Feb-97	Boykin, <i>et al.</i>	514	461	
	A26	5,605,811	Feb-97	Seubert, <i>et al.</i>	435	29	
	A27	5,606,058	Feb-97	Boykin, <i>et al.</i>	544	242	
	A28	5,612,363	Mar-97	Mohan, <i>et al.</i>	514	392	
	A29	5,622,955	Apr-97	Boykin, <i>et al.</i>	514	256	
	A30	5,627,184	May-97	Boykin <i>et al.</i>	514	256	
	A31	5,639,755	Jun-97	Dykstra, <i>et al.</i>	514	256	
	A32	5,643,562	Jul-97	Kisilevsky, <i>et al.</i>	424	78.31	
	A33	5,643,935	Jul-97	Dykstra, <i>et al.</i>	514	394	
	A34	5,667,975	Sep-97	Dykstra, <i>et al.</i>	435	6	
	A35	5,668,166	Sep-97	Tidwell, <i>et al.</i>	514	411	
	A36	5,668,167	Sep-97	Tidwell, <i>et al.</i>	514	411	
	A37	5,686,456	Nov-97	Boykin, <i>et al.</i>	514	256	
	A38	5,686,477	Nov-97	Jarry <i>et al.</i>	514	377	
	A39	5,686,496	Nov-97	Anderskewitz <i>et al.</i>	514	637	
Examiner				Date Considered			
<p>*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.</p>							

APPLICANT FACSIMILE OF FORM PTO-1449 REV 7-80	U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE	ATTY DOCKET NO NBI-105CN	SERIAL NO. 10/731,463
LIST OF PUBLICATIONS CITED BY APPLICANT (Use several sheets if necessary)		APPLICANT Chalifour, et al.	
		FILING DATE December 5, 2003	GROUP 1621

U.S. PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE
	B1	5,720,936	Feb-98	Wadsworth, et al.	424	9.1	
	B2	5,721,106	Feb-98	Maggio, et al.	435	7.8	
	B3	5,723,288	Mar-98	Dykstra et al.	435	6	
	B4	5,723,495	Mar-98	Hall, et al.	514	633	
	B5	5,726,197	Mar-98	Clark et al.	514	387	
	B6	5,728,375	Mar-98	Kisilevsky, et al.	424	78.31	
	B7	5,731,332	Mar-98	Anderskewitz et al.	514	354	
	B8	5,792,782	Aug-98	Dykstra, et al.	514	394	
	B9	5,811,633	Sep-98	Wadsworth et al.	800	12	
	B10	5,817,686	Oct-98	Dykstra, et al.	514	394	
	B11	5,817,687	Oct-98	Dykstra, et al.	514	394	
	B12	5,840,294	Nov-98	Kisilevsky, et al.	424	78.31	
	B13	5,843,980	Dec-98	Hall, et al.	514	438	
	B14	5,871,924	Feb-99	Yarus, et al.	435	6	
	B15	5,935,982	Aug-99	Dykstra, et al.	514	394	
	B16	5,939,440	Aug-99	Dykstra, et al.	514	338	
	B17	5,972,328	Oct-99	Kisilevsky, et al.	424	78.31	
	B18	5,972,969	Oct-99	Dykstra, et al.	514	338	
	B19	6,008,247	Dec-99	Boykin, et al.	514	471	
	B20	6,017,941	Jan-00	Dykstra, et al.	514	394	
	B21	6,025,398	Feb-00	Hall, et al.	514	633	
	B22	6,037,377	Mar-00	Anderskewitz et al.	514	635	
	B23	6,046,226	Apr-00	Dykstra, et al.	514	394	
	B24	6,127,423	Oct-00	Anderskewitz et al.	514	637	
	B25	6,127,554	Oct-00	Boykin, et al.	549	504	
	B26	6,133,281	Oct-00	Gonzalez-Cadavid et al.	514	289	
	B27	6,156,779	Dec-00	Dykstra, et al.	514	397	
	B28	2003/0130303	Jul-03	Coe, et al.	514	300	
	B29	6,172,104 B1	Jan-03	Tidwell, et al.	514	443	
	B30	6,197,824 B1	Mar-03	Schromm et al.	514	637	
	B31	6,214,883 B1	Apr-03	Hall, et al.	514	633	
	B32	6,294,565 B1	Sep-03	Dykstra, et al.	514	397	
	B33	6,319,944 B1	Nov-03	Claiborne, et al.	514	452	
	B34	6,326,395 B1	Dec-03	Tidwell, et al.	514	461	
	B35	6,489,365 B1	Dec-03	Anderskewitz et al.	514	637	
	B36	6,625,612 B1	Sep-03	Tal et al.	707	102	
	B37	6,627,647 B1	Sep-03	Betageri	514	333	

Examiner

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EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE
	C1	6,635,668 B1	Oct-03	Tidwell <i>et al.</i>	514	394	
	C2	US 20010044468 A1	Nov-03	Hall <i>et al.</i>	514	574	
	C3	US 20030083362 A1	May-03	Boykin <i>et al.</i>	514	408	
	C4	US 20030199521 A1	Oct-03	Dykstra <i>et al.</i>	514	256	

FOREIGN PATENT DOCUMENTS

		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION	
							YES	NO
✓	C5	JP 72-79092	Aug-72	Japan			Abstract	
✓	C6	EP 0 518 818 A2	Dec-92	EPO				
✓	C7	WO 93/16036 A1	Aug-93	WO				
✓	C8	WO 94/11341 A1	May-94	WO				
✓	C9	EP 0 601 977 A1	Jun-94	EPO				
✓	C10	EP 941991 B1	May-01	EPO				
✓	C11	WO 95/19772 A1	Jul-95	WO				
✓	C12	WO 96/15126 A1	May-96	WO				
✓	C13	WO 96/28187	Sep-96	WO				
✓	C14	WO 98/13037 A1	Apr-98	WO				
✓	C15	WO 98/40381 A1	Sep-98	WO				
✓	C16	WO 98/55454 A2	Dec-98	WO				
✓	C17	WO 00/04893 A2, A3	Feb-00	WO				
✓	C18	WO 01/03680	Jan-01	WO				
✓	C19	WO 01/03685 A2	Jan-01	WO				
✓	C20	WO 01/32159 A2	May-01	WO				
✓	C21	WO 01/46175 A1	Jun-01	WO				
✓	C22	WO 01/85093	Nov-01	WO				
✓	C23	WO 02/02516 A2	Jan-02	WO				
✓	C24	WO 02/34715 A1	May-02	WO				
✓	C25	WO 02/36588 A2	May-02	WO				
✓	C26	WO 02/55025 A2	Jul-02	WO				
✓	C27	WO 02/058684	Aug-02	WO				
✓	C28	WO 02/058697	Aug-02	WO				
✓	C29	WO 02/062785 A1	Aug-02	WO				
✓	C30	WO 03/103598 A2	Dec-03	WO				
✓	C31	WO 03/017994 A1	Mar-03	WO				
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APPLICANT FACSIMILE OF FORM PTO-1449 REV 7-80	U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE	ATTY DOCKET NO NBI-105CN	SERIAL NO. 10/731,463
LIST OF PUBLICATIONS CITED BY APPLICANT (Use several sheets if necessary)		APPLICANT Chalifour, et al.	
		FILING DATE December 5, 2003	GROUP 1621

OTHERS (including Author, Title, Date, Pertinent Pages, Etc.)

D1	✓	Askanas V, <i>et al.</i> , "New advances in the understanding of sporadic inclusion-body myositis and hereditary inclusion-body myopathies." <i>Curr. Opin. Rheumatol.</i> 7(6), 486-96 (1995 Nov).
D2	✓	Askanas V, <i>et al.</i> , "Transfer of beta-amyloid precursor protein gene using adenovirus vector causes mitochondrial abnormalities in cultured normal human muscle." <i>Proc. Nat'l Acad. Sci. U.S.A.</i> 93(3), 1314-19 (1996 Feb).
D3	✓	Bailly, C, <i>et al.</i> , Sequence-selective binding to DNA of bis(amidinophenoxy)alkanes related to propamidine and pentamidine. <i>Biochem J.</i> 1997 Apr 1;323 (Pt 1):23-31
D4	✓	Baldwin, <i>et al.</i> , "Research Advances," in <i>Alzheimer's Disease and Related Disorders</i> , John Wiley and Sons, New York, 757-773(1995).
D5	✓	Bayer, TA, <i>et al.</i> , "Key factors in Alzheimer's disease: β amyloid precursor protein processing, metabolism and intraneuronal transport," <i>Brain Pathology</i> 11, 111 (2001).
D6	✓	Beekes, M, <i>et al.</i> , "Western blot mapping of disease-specific amyloid in various animal species and humans with transmissible spongiform encephalopathies using a high-yield purification method." <i>J. Gen. Virol.</i> 76(Pt 10), 2567-76 (1995 Oct).
D7	✓	Benson, DA, <i>et al.</i> , <i>Nucl. Acids Res.</i> 28(1):15-18 (2000)
D8	✓	Berge, <i>et al.</i> , "Pharmaceutical salts." <i>J. Pharm. Sci.</i> 66(1), 1-19 (1977 Jan).
D9	✓	Bilik P., <i>et al.</i> , "Novel dications with unfused aromatic systems: trithiophene and trifuran derivatives of furimidazole," <i>CHEMBIOCHEM</i> 2(78), 559-69 (2001).
D10	✓	Boado, R.J., <i>et al.</i> , Drug delivery of antisense molecules to the brain for treatment of Alzheimer's disease and cerebral AIDS. <i>J. Pharm. Sci.</i> 87(11), 1308-15 (1998 Nov).
D11	✓	Bohrmann, B., <i>et al.</i> , Self-assembly of β -amyloid 42 is retarded by small molecular ligands at the stage of structural intermediates. <i>J. Struct. Biol.</i> 130(2-3), 232-46 (2000 Jun).
D12	✓	Boykin, D. W <i>et al.</i> , Anti-Pneumocystis carinii pneumonia activity of dicationic diaryl methylpyrimidines. <i>European Journal of Medicinal Chemistry</i> (1997), 32(12), 965-972.
D13	✓	Cardin, A.D, <i>et al.</i> , Molecular modeling of protein-glycosaminoglycan interactions. <i>Arteriosclerosis</i> . 9(1), 21-32 (1989 Jan-Feb).
D14	✓	Caughey, GH, <i>et al.</i> , Bis(5-amidino-2-benzimidazolyl)methane and related amidines are potent, reversible inhibitors of mast cell tryptases. <i>J Pharmacol Exp Ther.</i> 1993 Feb;264(2):676-82.
D15	✓	Chauhan, PM, <i>et al.</i> , Effect of new diamidines against Leishmania donovani infection. <i>Indian J Exp Biol.</i> 1993 Feb;31(2):196-8
D16	✓	Chongprasert, S., <i>et al.</i> , Effects of freeze-dry processing conditions on the crystallization of pentamidine isethionate. <i>J. Pharm. Sci.</i> 87(9), 1155-60 (1998 Sep).
D17	✓	Clercq ED, Dann O., Diaryl amidine derivatives as oncornaviral DNA polymerase inhibitors. <i>J Med Chem.</i> 1980 Jul;23(7):787-95
D18	✓	Contreras, J.M., <i>et al.</i> , "Aminopyridazines as acetylcholinesterase inhibitors." <i>J. Med. Chem.</i> 42(4), 730-41 (1999 Feb).
D19	✓	Czarny A, <i>et al.</i> , Analysis of van der Waals and Electrostatic Contributions in the Interactions of Minor Groove Binding Benzimidazoles with DNA <i>J. Am. Chem. Soc.</i> ; 1995; 117(16); 4716-4717
D20	✓	de Koning, EJ, <i>et al.</i> , "Diabetes mellitus in Macaca mulatta monkeys is characterised by islet amyloidosis and reduction in beta-cell population." <i>Diabetologia</i> 36(5), 378-84 (1993 May).
D21	✓	Donkor, IO, <i>et al.</i> , "Pentamidine congeners: 2,2-butenebridged aromatic diamidines and diimidazolines as potential anti-Pneumocystis carinii pneumonia agents," <i>J. Med. Chem.</i> 37(26), 4554-57 (1994).
D22	✓	Dubovi, EJ, <i>et al.</i> , Inhibition of respiratory syncytial virus-host cell interactions by mono- and diamidines. <i>Antimicrob Agents Chemother.</i> 1981 Apr;19(4):649-56
D23	✓	Dunbar PG, <i>et al.</i> , Design, synthesis, and neurochemical evaluation of 2-amino-5-(alkoxycarbonyl)-3,4,5,6-tetrahydropyridines and 2-amino-5-(alkoxycarbonyl)-1,4,5,6-tetrahydropyrimidines as M1 muscarinic receptor agonists. <i>J Med Chem.</i> 1994 Aug 19;37(17):2774-82
D24	✓	Fairley, TA, <i>et al.</i> , Structure, DNA minor groove binding, and base pair specificity of alkyl- and aryl-linked bis(amidinobenzimidazoles) and bis(amidinoindoles). <i>J Med Chem.</i> 1993 Jun 11;36(12):1746-53
D25	✓	Frangione, B, <i>et al.</i> , "Familial cerebral amyloid angiopathy related to stroke and dementia." <i>Amyloid</i> . 8(Suppl 1), 36-42, Review (2001 Jul).
D26	✓	Garcia-Sevilla J, <i>et al.</i> , I2-imidazoline receptors in the healthy and pathologic human brain. <i>Ann N Y Acad Sci.</i> 1995 Jul 12;763:178-93

Examiner

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OTHERS (including Author, Title, Date, Pertinent Pages, Etc.)

E1	✓	Garcia-Sevilla JA, "Imidazoline receptor proteins in brains of patients with Alzheimer's disease." <i>Neurosci. Lett.</i> 247(2-3), 95-98 (1998 May).
E2	✓	Geratz, JD, <i>et al.</i> , Amidino-substituted aromatic heterocycles as probes of the specificity pocket of trypsin-like proteases. <i>Arch Biochem Biophys.</i> 1979 Oct 15;197(2):551-9.
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E4	✓	Geratz, JD, <i>et al.</i> , Inhibitory effect of amidino-substituted heterocyclic compounds on the amidase activity of plasmin and of high and low molecular weight urokinase and on urokinase-induced plasminogen activation. <i>Thromb Res.</i> 1981 Oct 1-15;24(1-2):73-83
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F1	✓	Schauhan, P. M., Antiparasitic agents. Part VI. Synthesis of 1,2-, 1,3-, and 1,4-bis(4-substituted (aryloxy))benzenes and their biological activities Organic Chemistry Including Medicinal Chemistry (1988), 27B(1), 38-42
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F6	✓	Tidwell, RR, et al Strategies for anticoagulation with synthetic protease inhibitors. Xa inhibitors versus thrombin inhibitors. Thromb Res. 1980 Aug 1;19(3):339-49.
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